

REMARKS

The official action of 10 June 2009 has been carefully considered and reconsideration of the application as amended is respectfully requested.

Claims 12 and 16 have been amended to correct typographical errors. Claim 12 has also been amended in accordance with the description in the application as filed at, for example page 1, first paragraph, Example 11 on pages 15-16 and Fig. 8 of the drawings. Claims 31-33 have been canceled thereby rendering moot the rejection under 35 USC 102(b) appearing at page 3 of the official action.

The indicated allowability of claims 14 and 28-30 is noted with appreciation.

Claims 12-13, 15-18 and 31-39 stand rejected under 35 USC 103(a) as allegedly being unpatentable over Jin et al (1996) in view of Costa et al and Hogaboam et al. Applicants respectfully traverse this rejection.

The claimed invention is based at least in part upon Applicants' discovery that the administration of cardiotrophin-1 (CT-1) to a subject whose liver has suffered injury (as occurs, e.g., when functional liver mass is diminished or the liver is resected) can provide a therapeutic effect to the subject. In particular, Applicants found, unexpectedly, that not only does CT-1 prevent liver damage in healthy cells, it has anti-apoptotic activity that has a

therapeutic effect on injured livers.

To explain, in an injured liver, several hepatocyte populations might co-exist, depending on its level of damage: dead hepatocytes, damaged hepatocytes and non-affected (healthy) hepatocytes. Applicants found that CT-1 has regenerative activity that induces proliferation of new hepatocytes that can replace the dead ones and, equally and additionally crucial, it has anti-apoptotic activity that prevents death of injured and healthy hepatocytes in the presence of an agent toxic for the liver. Based on this discovery, the invention defined by the subject claims is directed to a method that treats subjects with injured livers, i.e., livers that have experienced a loss of functional liver cells.

The references cited by the Examiner do not provide even a reasonable expectation of success in the use of CT-1 to treat a subject with an injured liver, i.e., a subject whose liver has suffered a functional loss of liver cells, as discussed below. In the absence of a reasonable expectation of success in such treatment, the references cannot set forth even a *prima facie* case of obviousness for the invention defined by the subject claims. See MPEP 2143.02.

In an attempt to establish a reasonable expectation of success, the Examiner contends that: (a) Jin et al's disclosure that CT-1 induces liver growth *in vivo* demonstrates that CT-1 can stimulate hepatocyte proliferation and/or differentiation; and (b) the disclosure in Costa and Hogaboam that **different** proteins (i.e., proteins other than CT-1) that induce hepatocyte proliferation may be useful to treat subjects with liver damage provides a

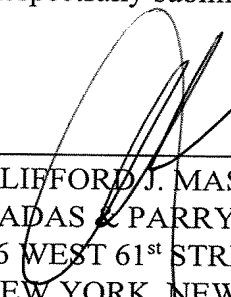
reasonable expectation that CT-1 would also be useful to treat subjects with liver damage. As discussed in the Declaration under 37 CFR 1.132 of one of the co-inventors, Matilde BUSTOS DE ABAJO, (submitted herewith), each of these contentions is respectfully flawed.

With respect to contention (a), the Declaration shows that there are a number of factors, other than proliferation or differentiation of hepatocytes, that could account for the increase in liver weight in the mice in the Jin et al study such that one of skill in the art could not have concluded that the increased liver weight was a result of hepatocyte proliferation or differentiation (see Declaration at paragraphs 5-7). Indeed, the Declaration shows that the increased weight described in Jin et al was likely **not** due to such proliferation.

With respect to contention (b), the Declaration cites other publications that show that one of skill in the art could not extend the teachings in Costa or Hogaboam to other, non-described proteins (such as CT-1) with even a reasonable expectation of success. See Declaration at paragraph 8. Accordingly, and since neither of the premises on which the Examiner bases her contention of a reasonable expectation of success can support such contention (see Declaration at paragraphs 5-9), Applicants respectfully submit that the references are incompetent to set forth even a *prima facie* case of obviousness for the invention as defined by the claims as amended.

In view of the above, Applicants respectfully submit that the prior art and all other rejections of record have been overcome and that the application is now in allowable form. An early notice of allowance is earnestly solicited and is believed to be fully warranted.

Respectfully submitted,



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